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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,454	08/29/2001	Dietrich A. Stephan	64688/153	5061

7590 09/22/2005

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EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/940,454	STEPHAN ET AL.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SBD

DETAILED ACTION

Applicants' arguments, filed 5/13/2005, have been fully considered and they are not deemed to be persuasive. The following rejections and/or objections are either reiterated or newly applied.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-27 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained from the previous office action.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The applicant has responded to this rejection by first referring to passages that the applicant contends support his position. However, the Examiner maintains that Collet et al. demonstrate that no quantitative relationship been sufficiently established to equate *in vitro* methods with *in vivo* methods. Collet et al. state, "Establishing quantitative relationships between *in vitro* and *in vivo* indicators will be useful in developing models that can predict the likely *in vivo* impact of drug-PGP interaction identified by reductive *in vitro* screens." (emphasis added) (page 825, left column) While Collet et al. may have establish one of many parameters to correlate *in vitro* with *in vivo* correlation of PGP function, Collet et al. still recognizes that the correlation has not been fully developed. Furthermore, even with a correlation model, it can only predict the likely *in vivo* impact. It certainly would not predict with certainty that drug would inhibit or reverse metastasis.

Next the applicant refers to two papers by John M. Weinstein, MD, PhD and Michael R. Boyd, MD, PhD regarding the validity of using cell lines to screen for potential drug targets. However neither article claims that *in vitro* studies are an accurate prediction of the effects of a drug *in vivo*. On the first page, Dr. Weinstein's article, he states, "Cell lines in culture do not fully reflect cells *in vivo*, of course, but, historically most of our knowledge of molecular pharmacology and targets has come from cultured cells, not clinical material." The Examiner does not dispute that

information may be gleaned from *in vitro* studies, however obtaining information from *in vitro* studies does not equate to predicting *in vivo* effects.

Finally the applicant cites *In re Brana* to support his argument. However, it is unclear to the Examiner how these citations support the Applicant's arguments. The court merely concludes that those models represented a disease, not that models were the equivalent of the *in vivo* version of the disease. The Examiner agrees that the majority of *in vitro* studies represent some sort of biological process, however that does not mean that these studies are necessarily the equivalent to the *in vivo* version.

Furthermore, it remains that the specification contains no disclosure of the correlation between the *in vitro* studies and any *in vivo* use. Without such correlation or the actual *in vivo* studies, one of skill in the art would not recognize that the applicant was enabled for use *in vivo*. In addition, contacting a substance *in vivo* is subject to a variety of factors, which may cause unexpected results.

This rejection is newly applied to new claims 26 and 27 as necessitated by amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 18, 20- 22, 26, and 27, are rejected under 35 U.S.C. 102(b) as being anticipated by Zujewski et al.

This rejection is maintained from the previous office action and newly applied to new claims 26 and 27.

The applicant responded Zujewski et al. only discloses toxicity studies. The Examiner disagrees. As it was cited in the previous action, on page 939, the paragraph bridging column 1 and 2, Zujewski et al. states, "Pharmacokinetic studies demonstrate that 500 mg orally twice daily achieves plasma concentrations correlating with an antitumor effect in preclinical studies." Zujewski et al. does disclose the effect on tumors.

The applicant also responded that the main target of the present invention is PDGFRA. However, the instant claims are not so limited. The Examiner must read the claims as broadly as possible. Given that this limitation is not in the claims, the applicant's response is irrelevant.

The applicant has also amended claim 18. However, the practice of claim 18 does not require these additional limitations. The practice of claim 18 only requires that a gene that is associated with M+ class be inhibited. The amendments to claim 18 only provide the process of gene identification, however the gene is product of this process. According to the MPEP §2113, product by process claims are not limited to the

manipulations of the recited steps, only the structure implied by the steps. Thus, instant claim 18 is still anticipated by the Zujewski et al. reference.

Zujewski et al. is newly applied to new claims 26 and 27. Zujewski et al. teach using a R115777, which is an inhibitor of *RAS* gene, which is a gene downstream of the PDGFRA gene (See Abstract).

Claims 18-21 and 23-25 remain rejected under 35 U.S.C. 102(e)(2) as being anticipated by Daley.

The applicants states that Daley is irrelevant because it discusses solely the use of inhibitors of farnesyl protein transferase. The Examiner disagrees. As was cited in the previous office action, Daley states, "Two primary approaches have been taken to block growth receptor signaling pathways . . . antisense nucleic acids to block protein expression." Daley does disclose inhibiting a gene associated with M+ class and is relevant.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 6:30-5:00, M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199.

Ardin H. Marschel 9/18/05
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

JL